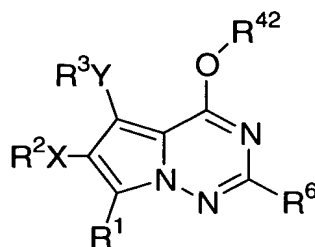


**What is Claimed is:**

1. A process for preparing a compound of formula (I)



(I)

wherein

X and Y are independently selected from O, OCO, S, SO, SO<sub>2</sub>, CO, CO<sub>2</sub>, NR<sup>10</sup>, NR<sup>11</sup>CO, NR<sup>12</sup>CONR<sup>13</sup>, NR<sup>14</sup>CO<sub>2</sub>, NR<sup>15</sup>SO<sub>2</sub>, NR<sup>16</sup>SO<sub>2</sub>NR<sup>17</sup>, SO<sub>2</sub>NR<sup>18</sup>,

10 CONR<sup>19</sup>, halogen, nitro, cyano, or X or Y are absent;

R<sup>1</sup> is hydrogen;

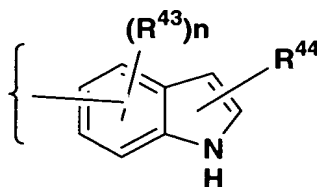
R<sup>2</sup> and R<sup>3</sup> are independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, aralkyl, substituted aralkyl, heteroaryl, substituted heteroaryl, 15 heterocycloalkyl or substituted heterocycloalkyl; with the proviso that when X is halo, nitro or cyano, R<sup>2</sup> is absent, and, when Y is halo, nitro or cyano, R<sup>3</sup> is absent;

R<sup>6</sup> is H;

R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup>, R<sup>13</sup>, R<sup>14</sup>, R<sup>15</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>18</sup> and R<sup>19</sup> are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl,

20 substituted aryl, heteroaryl, substituted heteroaryl, heterocyclo, or substituted heterocyclo;

R<sup>42</sup> is



$(R^{43})_n$  wherein n equals 0, 1 or 2 and each  $R^{43}$  is independently selected from the group consisting of hydrogen, fluorine, chlorine and methyl; and

$R^{44}$  is methyl, or hydrogen,

5 with the further provisos that:

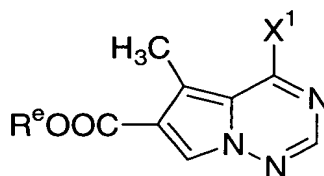
a.  $R^2$  may not be hydrogen if X is SO, SO<sub>2</sub>, NR<sup>13</sup>CO<sub>2</sub>, or NR<sup>14</sup>SO<sub>2</sub>; and

b.  $R^3$  may not be hydrogen if Y is SO, SO<sub>2</sub>, NR<sup>13</sup>CO<sub>2</sub>, or NR<sup>14</sup>SO<sub>2</sub>;

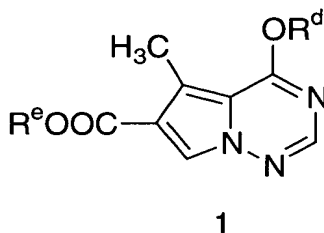
or an enantiomer, diastereomer, or pharmaceutically acceptable salt, prodrug, or solvate thereof,

10 which comprises the steps of

a) converting a compound of the formula



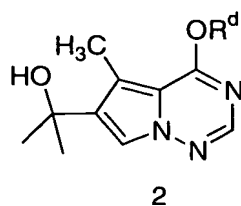
15 where  $R^e$  is lower alkyl or aryl and  $X^1$  is a halogen to a compound 1 of the formula



where  $R^d$  is lower alkyl, aryl, substituted aryl, heteroaryl or substituted heteroaryl, by

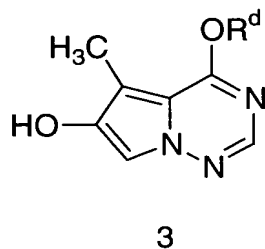
20 treatment with a phenoxide, or alkoxide,

b) alkylating Compound 1 to afford Compound 2 of the formula



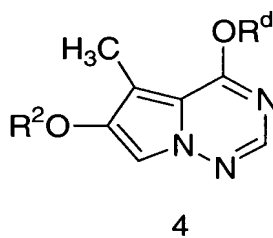
c) treating compound 2 with a peroxide in the presence of a Lewis acid to afford compound 3 of the formula

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d) alkylating the phenol group in compound 3 to afford Compound 4 of the formula

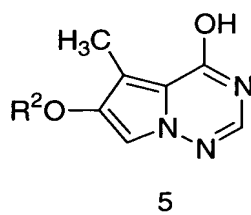
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where R<sup>2</sup> is benzyl or substituted benzyl,

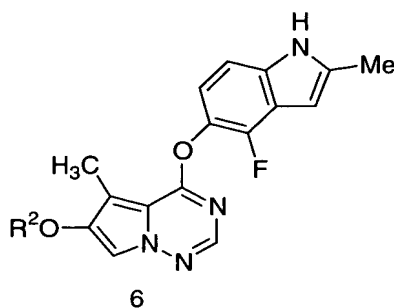
e) hydrolyzing Compound 4 to afford Compound 5 of the formula

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where  $R^2$  is benzyl or substituted benzyl, and

- f) converting Compound 5 to Compound 6 of the formula



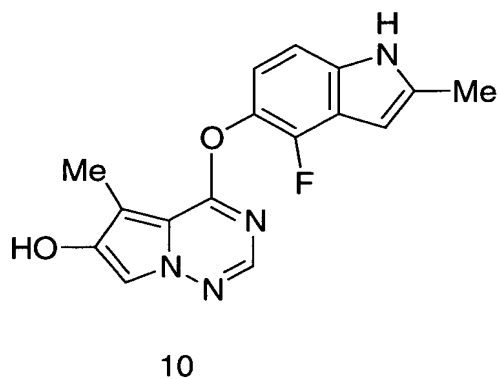
5

by first converting compound 5 to a chloroimidate, subsequently alkylating the chloroimidate to afford Compound 6 wherein  $R^2$  is benzyl and deprotecting the phenol by treatment with a hydrogen donor in the presence of a catalyst to afford compound 6 where  $R^2$  is hydrogen.

10

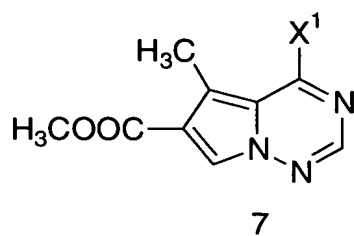
2. The process according to Claim 1 wherein in step c), hydrogen peroxide is used in the presence of a Lewis acid to convert the benzylic alcohol to the phenol.

- 15 3. A process for preparing a compound of the formula



which comprises the steps of

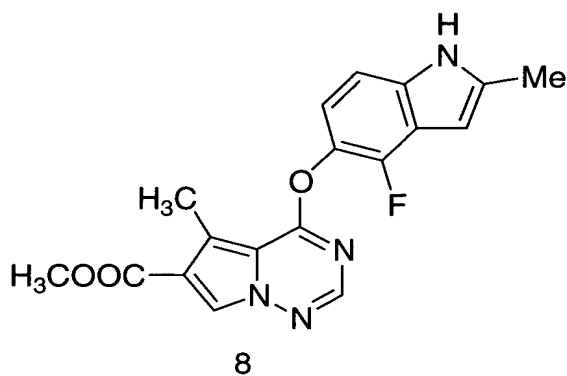
- 20 a) reacting a compound of the formula



where  $X_1$  is halogen;

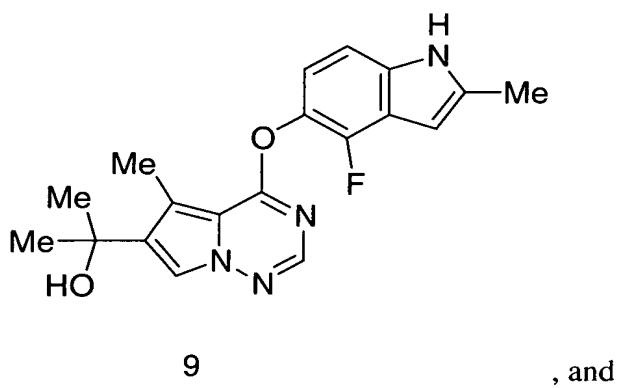
with a nucleophile to afford Compound 8 of the formula

5



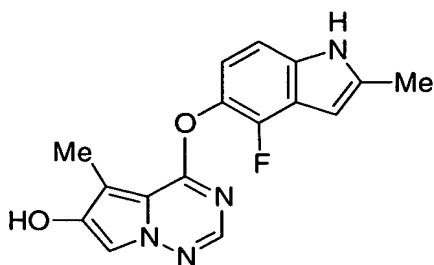
b) treating Compound 8 with an alkylating agent at low temperature, to afford Compound 9 of the formula

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c) treating Compound 9 with a peroxide in the presence of a Lewis acid to afford Compound 10 of the formula

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4. The process according to Claim 3 wherein the alkylating agent in step (b) is an alkyl magnesium halide.

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5. The process according to Claim 4 wherein the alkyl magnesium halide is methyl magnesium bromide or methyl magnesium chloride.

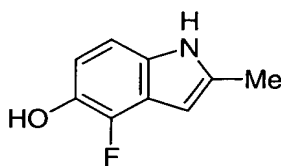
6. The process according to Claim 4 wherein the peroxide used in step c) is hydrogen peroxide or sodium perborate.

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7. The process according to Claim 4 wherein the Lewis acid used in step c) is boron trifluoride.

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8. A process for preparing a compound of the formula

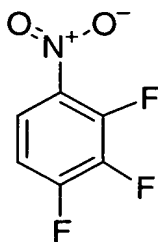


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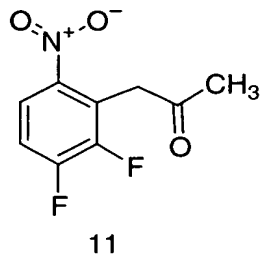
which comprises the steps of

20

a) reacting a fluorinated compound of the formula

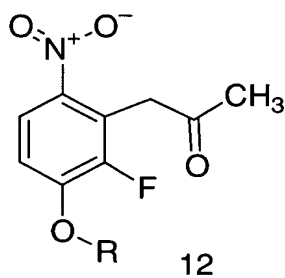


b) with a nucleophile to afford Compound 11 of the formula



5

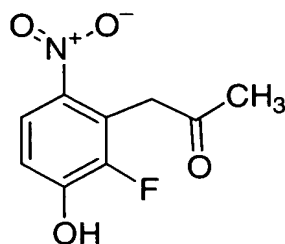
c) reacting Compound 11 with an alkoxy anion to afford Compound 12 of the formula



10

wherein R is a protecting group,

d) deprotecting the alkoxy group by treatments with deprotecting reagents  
15 to afford Compound 13 of the formula

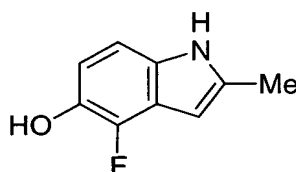


13 , and

e) cyclizing Compound 13 under reducing conditions to afford Compound

14 .

5



14

9. The process according to Claim 8 wherein the reduction in step (e) utilizes sodium dithionite in water or a mixture of water and an organic solvent such as THF.

10. The process according to Claim 8 wherein the reduction in step (d) utilizes pyridinium chloride or pyridinium iodide or hydrogen bromide.

11. A pharmaceutical composition comprising at least one or more compounds of Claim 1 in combination with a pharmaceutically acceptable carrier and at least one additional anti-cancer or cytotoxic agent.

12. A method for producing an antiangiogenic effect which comprises administering to a mammalian species in need thereof, an effective antiangiogenic producing amount of at least one compound made by the process of Claim 1.

13. A method for producing a vascular permeability reducing effect which comprises administering to a mammalian species in need thereof an effective vascular

permeability reducing amount of at least one compound made by the process of Claim 1.

14. A method of inhibiting protein kinase activity of growth factor receptors  
5 which comprises administering to a mammalian species in need thereof, an effective protein kinase inhibiting amount of at least one compound made by the process of Claim 1.

15. A method of inhibiting tyrosine kinase activity of growth factor  
10 receptors which comprises administering to a mammalian species in need thereof, an effective tyrosine kinase inhibiting amount of at least one compound made by the process of Claim 1.

16. A method for treating diseases associated with signal transduction  
15 pathways operating through growth factor receptors, which comprises administering to a mammalian species in need thereof a therapeutically effective amount of at least one compound made by the process of Claim 1.